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Dopaminergic Pathways and Their Role in Medication-Overuse Headache: behavioral or analgesic?

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Introduction

With an estimated prevalence of up to 2% worldwide, medication-overuse headache (MOH) is defined by the International Classification of Headache Disorders 3rd edition (ICHD-3) as a secondary headache, occurring 15 or more days per month, result from a deterioration of a pre-existing headache due to medication use excessive use of acute headache medications for more than 3 months. It is an important factor in the chronicity of primary headaches and its pathophysiology remains under investigation.

Objective

To evaluate the evidence linking dopaminergic dysfunction to the pathophysiology of MOH and determine whether dopamine's role is analgesic, behavioral or both.

Methodology

A comprehensive literature search was conducted using PubMed and Virtual health Library (VHL) Regional Portal as databases, with the descriptors "dopamine" and "medication overuse headache." Inclusion criteria were studies addressing dopaminergic pathways, receptor involvement or neuroimaging findings related to MOH. Therefore, fifteen articles were evaluated.

Results

Genetic studies have found reduced expression of dopamine D2 receptors (DRD2) and dopamine metabolism in patients with MOH, with defects in tyrosine-beta-hydroxylase, resulting in higher levels of available dopamine. Neurofunctionally, the main dopaminergic pathway affected is the mesocorticolimbic pathway (known as the reward system region), with dysfunctions also present in the nigrostriatal pathway. Neuroimaging studies showed reduced activity in the substantia nigra/ventral tegmental area (SN/VTA) and increased activity in the ventromedial prefrontal cortex (VMPFC) in MOH patients, similar do addictions, indicating a link between medication overuse and dopaminergic dysfunction. This scenario points to a behavioral impact, with a greater predisposition to impulsivity and the maintenance of excessive medication consumption, favoring the chronification of the headache. Although medications that act to modulate dopaminergic activity – such as chlorpromazine – are described in the literature, the few studies that demonstrate the analgesic action related to dopamine do so indirectly through their action on prolactin levels and prevention of nociceptor sensitization.

Conclusion

Studies suggest the presence of dopaminergic dysfunction in MOH, especially in the mesocorticolimbic pathway. The findings suggest a mainly behavioral impact of dopamine in controlling the disease, with the potential for treatment strategies that assist in more effective management of MOH.